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Inhibitory effects of kratom leaf extract (*Mitragyna speciosa* Korth.) on the rat gastrointestinal tract

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Abstract

Kratom (*Mitragyna speciosa* Korth.) is an indigenous plant of Thailand used traditionally in folk medicine although it is claimed to cause addiction. It is used to treat diarrhea, however, there is no scientific evidence to support the use. The aim of this study is to investigate the effect of methanolic extract of kratom leaves on the rat gastrointestinal tract. Kratom extract at 50, 100, 200 and 400 mg/kg (p.o.) caused a dose dependent protection against castor oil-induced diarrhea in rats and also inhibited intestinal transit. The antidiarrheal effect was not antagonized by naloxzone. The inhibition of intestinal transit by kratom extract was significantly different from the control when treated with a single dose for 1 day. For longer-term treatments of 15 and 30 days, kratom extract did not decrease the intestinal transit time indicating that adaptation had occurred. Kratom extract at a dose level of 200 and 400 mg/kg for 30 days and morphine at 3 mg/kg (i.p.) caused a decrease in the increment of body weight that was significantly different from the control and kratom extract at lower doses (50 and 100 mg/kg). However it had no effect on the level of plasma cholecystokinin. The results suggested that methanolic kratom extract exhibited its antidiarrheal effect on rat gastrointestinal tract. The effects may occur via pathways in addition to the action on opioid receptors. High does of kratom extract decreased the increment of body weight similar to the effect of morphine.
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Keywords: *Mitragyna speciosa*; Kratom; Diarrhea; Intestinal transit; Body weight; Cholecystokinin; CCK

1. Introduction

Mitragyna speciosa Korth., family Rubiaceae, is found in tropical and sub-tropical regions of Asia. It is a tree indigenous to Thailand, where it is mostly called kratom. It can be found throughout the country but is grown mostly in the southern region. To our knowledge, there are two varieties of kratom in Thailand, one with red veins in the leaf, the other with green veins. The red veined variety is supposed to have the stronger biological activities. Kratom has been traditionally used in Thailand and Malaysia. In addition to being used in its own right, as a narcotic drug, it is often used as a substitute for opium when opium is unavailable, or drug users are trying to moderate their opium addiction. A kratom user mostly likes to chew fresh leaves. When preparing fresh leaves, the vein is removed. Kratom has been reported to be a central nervous system stimulant rather than a depressant. It also helps to increase work efficiency and tolerance to hard work under a scorching sun (Suwanlert, 1975). Although the growing and harvesting of kratom is prohibited in Thailand, it is still used in traditional medicine and its use is still widespread especially where the kratom trees grow naturally.

Over 25 alkaloids have been isolated from kratom leaves. Mitragynine is the major alkaloid found in this plant. Mitragynine has been demonstrated to produce an antinociceptive effect through an action on supraspinal opioid receptors and descending noradrenergic and serotonergic systems (Matsumoto et al., 1996). Mitragynine inhibited the vas deferens contraction elicited by nerve stimulation, probably through its blockage of neuronal Ca^{2+} channels (Matsumoto et al., 2005). Mitragynine

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also inhibited guinea pig ileum contraction *in vitro* via the opioid receptors (Watanabe et al., 1997).

Kratom use is illegal in Thailand, Myanmar, Malaysia, Vietnam and, most recently, Australia. In contrast to these countries, kratom use remains uncontrolled in most of the world. It can be purchased at a wide variety of shops online. To our knowledge, it is not illegal to posess kratom, or use and grow it in all of Europe and the United States. Kratom leaves are often consumed fresh. Dried leaves can also be used in powder form, either swallowed or made into a tea that is strained and then drunk. In folk medicine, it is often used to treat diarrhea or intestinal infections by amoeba and protozoa (Chuakul et al., 1995). It was of interest therefore, to study the *in vivo* effect of a crude methanolic extract of kratom leaves on the gastrointestinal tract of rats.

2. Materials and methods

2.1. Plant material

Kratom leaves were collected from Satoon Province, in the southern part of Thailand during the months of February–May. A specimen of this plant was deposited at the PSU Herbarium of the Department of Biology, Faculty of Science, Prince of Songkla University, Thailand with the specimen voucher number PSU 012821.

2.2. Preparation of the methanolic extract

Air-dried leaves were pulverized by grinding, and then macerated twice in absolute methanol for 7 days, with stirring 2–3 times/day at room temperature. The extracts were filtered then mixed and concentrated using a rotary evaporator (Buchi, B169 Vacuum-System, Switzerland). Then they were freeze-dried (Corrosion Resistant Freezer Drier, FTS System Inc., USA). The yield from the methanolic extract of kratom leaves was 7.92% (w/w).

2.3. Experimental animals

Adult Wistar rats, weighing 200–250 g, were obtained from the Southern Laboratory Animal Facility, Prince of Songkla University. They were housed in a temperature controlled room at 25 ± 2 °C with a relative humidity of 50 ± 5% and a 12 h light/12 h dark cycle. They were fed with animal food pellets and water *ad libitum*. The study protocol was approved by the Animal Ethical Committee, Prince of Songkla University.

2.4. Castor oil-induced diarrhea

Castor oil was fed to rats to induce diarrhea as previously described by Atta and Mouneir (2004) with some modifications. Briefly, the rats were fasted for 24 h during which the drinking water was provided *ad libitum*. Each rat was randomly placed in a cage lined at the bottom with a transparent sheet. The rats were divided into 6 groups, 10 rats per group. Each rat received 2 mL of castor oil orally, 1 h before commencement of the experiment. In group 1, the rats were administered with the solvent vehicle only at 10 mL/kg. The solvent vehicle for dissolving the test material was prepared by mixing propylene glycol:tween 80:distilled water (4:1:4) and diluted with distilled water to 1:10. In groups 2–5, the rats were given orally 10 mL/kg of the methanolic extract of kratom dissolved in solvent vehicle in doses of 50, 100, 200 and 400 mg/kg, respectively. In group 6, the rats were orally administered 6 mg/kg of loperamide. The severity of the diarrhea was noted and recorded as scores using the method of Di Carlo et al. (1994). The scoring data were '++' for copious, '+' for mild (semisolid feces) and '0' for normal feces or lack of diarrhea. The total diarrheal score was calculated by summing the frequency of defecation in each score of '++', '+' and '0' multiplied by 2, 1 and 0, respectively. The fecal matter was collected and weighed over the total observation period of 8 h. The changes in body weight between the pre- and post-experiment were also determined.

2.5. Intestinal transit and intestinal fluid

Each rat in six groups was orally administered 2 mL of castor oil as previously described in Section 2.4. The rats were also given 10% activated charcoal in physiological saline in a volume of 3 mL/kg, 30 min after being given kratom extract and loperamide. The intestinal transit and volume of intestinal fluid in rats were measured as described by Di Carlo et al. (1994) with some modifications. The rats were anesthetized 15 min later by inhalation of ether and euthanized by cervical dislocation. The small intestine from the pylorus to the caecum was dissected. The distance of the charcoal plug from pylorus to ileum was determined and expressed as a percentage of the total length of the small intestine. The intestinal content was expelled into a Petri dish and its volume was measured using a measuring cylinder.

2.6. Body weight, intestinal transit and plasma cholecystokinin

Eighteen groups of rats were used, with 10 rats in each group. The rats in groups 1–3 were given solvent vehicle (p.o., 10 mL/kg) for 1, 15 and 30 days. In groups 4–15, the rats were administered the methanolic extract of kratom at the doses 50, 100, 200 and 400 mg/kg (p.o.) for 1, 15 and 30 days. In groups 16–18, the rats were injected with morphine intraperitoneally at the dose of 3 mg/kg for 1, 15 and 30 days. The body weight of each rat was recorded daily on each morning throughout the experiment. The rats were fasted for 24 h but given water *ad libitum* before the commencement of the experiment. All rats then received 3 mL/kg of 10% activated charcoal in physiological saline (p.o.) 1 h after being given the last dose of kratom extract. Animals were anesthetized by inhalation of ether, 15 min after charcoal administration. Blood was collected from the orbital plexus for cholecystokinin (CCK) assay. The animals were then euthanized by cervical dislocation. The abdomen was opened and small intestine was carefully removed. The distance traveled by the charcoal plug from the pylorus was measured and expressed as a percentage of the total length of the small intestine for each animal (Di Carlo et al., 1994).

2.7. Processing of plasma for CCK analysis

Rats were anesthetized by inhalation of ether. Blood samples (3 mL) were then collected from the orbital plexus and transferred into polypropylene tubes containing EDTA (1 mg/mL of blood) and aprotinin (500 KIU/mL of blood). Plasma was immediately obtained by centrifugation at 1600 × *g* for 15 min at 0 °C and stored at −70 °C until the assay for CCK. The concentration of CCK in the plasma samples were examined as described previously by Doong et al. (1998). In brief, a plasma sample (1 mL) was acidified with an equal volume of buffer A (1% trifluoroacetic acid) and centrifuged at 10,000 × *g* for 20 min at 4 °C. The supernatant was then loaded onto a pretreated Sep-Pak® Vac C18 cartridge (Waters Corporation, Milford, Mass, USA). Before use, the cartridge was equilibrated with 1 mL buffer B (60% acetonitrile in 1% trifluoroacetic acid and 39% distilled water) followed by buffer A (3 mL, three times). After loading plasma, the cartridge was slowly washed with buffer A (3 mL, twice) and the wash discarded. The peptide was slowly eluted from the cartridge with buffer B (3 mL, once) and the eluant collected in a polypropylene tube. The eluant was then freeze-dried (FTS System Inc., USA) and stored at −70 °C until used. The dry sample was reconstituted with an assay buffer before radioimmunoassay.

2.8. CCK analysis

The CCK concentration in the plasma samples was determined using the RIA kit purchased from Peninsula Laboratories, CA, USA. The radioactivity of the assay tube was measured in a gamma counter (Isocomp I, MGM Instruments Inc., USA).

2.9. Naloxone on the effect of kratom extract

Diarrhea was induced in rats by orally administering castor oil (2 mL) as previously described in Section 2.4. The rats were then given kratom extract orally at doses of 100, 200 and 400 mg/kg with or without pretreatment with naloxone (5 mg/kg, i.p.) for 30 min. The defecation frequency, total score, fecal weight and change in body weight were then recorded.

2.10. Data and statistical analysis

Results were expressed as the mean ± S.E.M. Significant differences were analysed by ANOVA, SPSS PC v.11.5 for windows followed by a Tukey comparison test for comparison of more than two groups. A probability level of less than 5% was considered significant. The percent inhibition of defecation score and fecal weight was calculated by (mean control − mean treated)/mean control × 100.

3. Results

3.1. Effect of methanolic extract of kratom leaves on castor oil-induced diarrhea

The methanolic extract of kratom leaves reduced defecation frequency, total score and fecal weight in castor oil-induced diarrheal rats in a dose dependent manner (Table 1). The kratom extract at the dose 100–400 mg/kg (p.o.) caused a significant decrease in the defecation frequency (when the severity of diarrhea was in the range of score '++'), total score and fecal weight as compared to the control ($P < 0.05$). Loperamide (6 mg/kg), used as a standard drug, also had an antidiarrheal activity, as was shown by a significant reduction in defecation frequency, total score and fecal weight from the control ($P < 0.05$). The antidiarrheal effect of loperamide was not significantly different from that of the kratom extract (100–400 mg/kg). This diarrheal model caused a reduction of rat body weight in every group but the reduction was not significantly different. Kratom (50–400 mg/kg) reduced the defecation score '++' (0–85.19%), the total score (2.63–85.09%) and fecal weight (24.18–88.15%). The percent inhibition of defecation score '++', total score and fecal weight caused by kratom extract were dose dependent (Fig. 1).

3.2. Effect of kratom extract on intestinal fluid and intestinal transit

Kratom extract (50–400 mg/kg) was shown to inhibit intestinal transit (33.90 ± 2.27% to 1.61 ± 0.97%) in a dose dependent manner (Table 2). This effect of the extract at the dose

Table 1
Effect of Kratom extract (50–400 mg/kg) and loperamide (6 mg/kg) on defecation frequency, total score, fecal weight and percent change in body weight after castor oil-induced diarrhea in rats

Treatment	Defecation frequency			Total score		Fecal weight		Change in BW (%)
	++	+	0	Score	Inhibition (%)	g	Inhibition (%)	
Control	5.40 ± 0.66^{a}	0.60 ± 0.22^{a}	0.30 ± 0.21	11.40 ± 1.35^{a}	0	8.52 ± 0.76^{a}	0	−0.81 ± 0.59
MS 50 mg/kg	5.40 ± 1.03^{a}	0.30 ± 0.15	0.20 ± 0.13	11.10 ± 2.09^{a}	2.63	6.46 ± 1.28^{a}	24.18	−0.18 ± 0.54
MS 100 mg/kg	1.90 ± 0.48^{b}	0.10 ± 0.10	0.20 ± 0.13	3.90 ± 0.95^{b}	65.79	2.37 ± 0.56^{b}	72.18	−0.73 ± 0.68
MS 200 mg/kg	1.50 ± 0.73^{b}	0.20 ± 0.13	0.20 ± 0.13	3.20 ± 1.43^{b}	71.93	1.94 ± 0.82^{b}	77.23	−0.77 ± 1.00
MS 400 mg/kg	0.80 ± 0.44^{b}	0.10 ± 0.10	1.50 ± 0.89	1.70 ± 0.87^{b}	85.09	1.01 ± 0.42^{b}	88.15	−0.28 ± 0.38
Loperamide 6 mg/kg	0.20 ± 0.20^{b}	0^{b}	0^{b}	0.40 ± 0.40^{b}	96.49	0.10 ± 0.10^{b}	98.83	−0.80 ± 1.08

Values are mean ± S.E.M., $n = 10$. BW, body weight; g, gram; MS, the methanolic extract of Kratom leaves; ++, copious feces; +, semisolid feces; 0, normal feces.

[a] Significant different from loperamide ($P < 0.05$).

[b] Significant different from the control ($P < 0.05$).

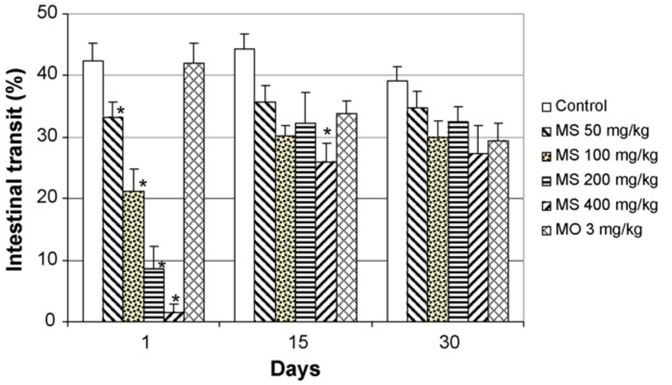

Fig. 1. Effect of kratom extract (50–400 mg/kg, p.o.) and morphine (3 mg/kg, i.p.) administration for the periods of 1, 15 and 30 days on intestinal transit in rats. Values are mean ± S.E.M., $n = 10$. MS, the methanolic extract of kratom leaves; MO, morphine. *Significantly different from the control at $P < 0.05$.

Table 2
Effect of kratom extract (50–400 mg/kg) and loperamide (6 mg/kg) on intestinal transit (%) and volume of intestinal fluid in the castor oil-induced diarrhea in rats

Treatment	Intestinal transit (%)	Intestinal fluid (mL)
Control	43.31 ± 2.94[a]	1.89 ± 0.22
MS 50 mg/kg	33.90 ± 2.27[a]	1.84 ± 0.21
MS 100 mg/kg	22.79 ± 3.05[a,b]	1.79 ± 0.27
MS 200 mg/kg	10.14 ± 3.48[b]	1.59 ± 0.15
MS 400 mg/kg	1.61 ± 0.97[b]	1.25 ± 0.08
Loperamide 6 mg/kg	1.40 ± 0.80[b]	1.20 ± 0.06

Values are mean ± S.E.M., $n = 10$. MS, the methanolic extract of kratom leaves.
[a] Significant different from loperamide ($P < 0.05$).
[b] Significantly different from the control ($P < 0.05$).

of 100–400 mg/kg were significantly different from the control ($P < 0.05$). However, the extract at all doses tested and loperamide had no effect on the intraluminal fluid volume. Loperamide (6 mg/kg) also inhibited the intestinal transit and it was significantly different from the kratom extract for the doses of 50 and 100 mg/kg ($P < 0.05$).

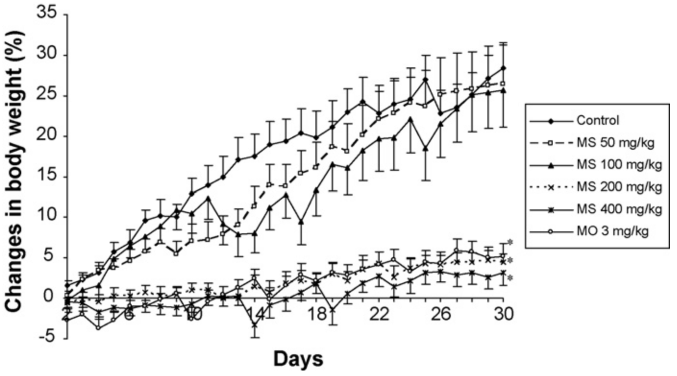

Fig. 2. Long-term treatment (30 days) of kratom extract (50–400 mg/kg, p.o.) and morphine (3 mg/kg, i.p.) on the percentage change in rat body weight. Values are mean ± S.E.M., $n = 10$. MS, the methanolic extract of kratom leaves; MO, morphine. *Significanly different from the control ($P < 0.05$).

3.3. *Effect of naloxone on the effect of kratom extract*

The results obtained from the evaluation of the antidiarrheal activity of kratom extract (100–400 mg/kg, p.o.) with or without pretreatment with naloxone are shown in Table 3. Pretreatment with naloxone at the dose of 5 mg/kg (i.p.) had no effect on the inhibition of kratom extract on defecation frequency, total score and fecal weight.

3.4. *Effect of kratom extract on intestinal transit in the periods of 1, 15 and 30 days*

The effect of kratom extract (50–400 mg/kg, p.o.) and morphine (3 mg/kg, i.p.) on intestinal transit was shown in Fig. 1. A single dose of kratom extract (day 1) decreased intestinal transit in a dose dependent manner (33.14 ± 2.56% to 1.53 ± 1.28%). Repeated doses of kratom extract for 15 and 30 days, however, had no effect on intestinal transit with the exception of the dose of 400 mg/kg for 15 days which significantly decreased intestinal transit as compared to the control ($P < 0.05$). Morphine did not affect intestinal transit.

Table 3
Effect of kratom extract (100–400 mg/kg, p.o.) with or without pretreatment with naloxone (5 mg/kg, i.p.) on defecation frequency, total score, fecal weight and percent change in body weight after castor oil-induced diarrhea in rats

Treatment	Defecation frequency			Total score		Fecal weight		Change in BW (%)
	++	+	0	Score	Inhibition (%)	g	Inhibition (%)	
Control	4.10 ± 1.24	1.30 ± 0.21	0.80 ± 0.41	12.00 ± 2.77	0	4.09 ± 0.64	0	−2.30 ± 0.28
Naloxone 5 mg/kg	3.70 ± 0.68	1.10 ± 0.35	0.80 ± 0.35	11.20 ± 1.37	6.67	3.10 ± 0.49	24.21	−2.08 ± 0.68
MS 100 mg/kg	2.00 ± 0.52	2.20 ± 0.44	0.40 ± 0.17	6.20 ± 1.36	48.33	2.14 ± 0.34	47.68	−2.26 ± 0.29
Nal + MS 100 mg/kg	3.60 ± 0.43	1.70 ± 0.42	1.00 ± 0.22	8.90 ± 1.02	25.83	2.91 ± 0.35	28.85	−2.80 ± 0.28
MS 200 mg/kg	1.40 ± 0.56	1.40 ± 0.48	0.20 ± 0.14	4.20 ± 1.15	65.00	1.82 ± 0.50	55.50	−2.29 ± 0.19
Nal + MS 200 mg/kg	1.20 ± 0.44	1.50 ± 0.48	0.20 ± 0.14	3.90 ± 0.84	67.50	1.60 ± 0.45	60.88	−1.81 ± 0.31
MS 400 mg/kg	1.13 ± 0.40	0.88 ± 0.40	0.60 ± 0.47	3.13 ± 0.93	73.92	1.35 ± 0.36	66.99	−2.14 ± 0.25
Nal + MS 400 mg/kg	1.50 ± 0.57	1.00 ± 0.27	0.200.16	4.00 ± 1.13	66.67	1.96 ± 0.47	52.08	−3.21 ± 0.34

Values are mean ± S.E.M., $n = 10$. Nal, naloxone; BW, body weight; g, gram; MS, the methanolic extract of kratom leaves; ++, copious feces; +, semisolid feces; 0, normal feces.

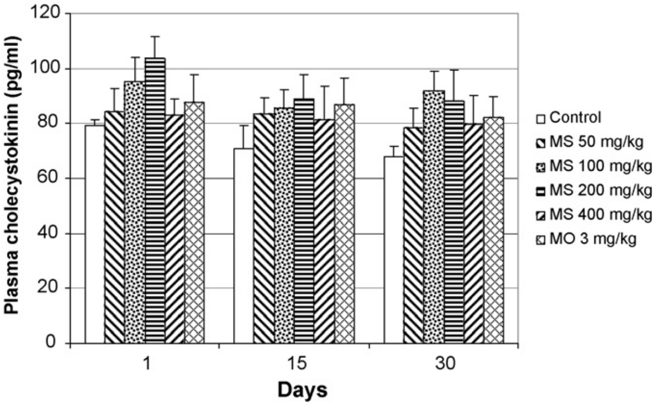

Fig. 3. Effect of kratom extract (50–400 mg/kg, p.o.) and morphine (3 mg/kg, i.p.) for the periods of 1, 15 and 30 days on plasma cholecystokinin in rats. Values are mean ± S.E.M., $n = 10$. MS, the methanolic extract of kratom leaves; MO, morphine.

3.5. *Effect of kratom extract on body weight*

The effect of long-term treatment (30 days) of kratom extract (50–400 mg/kg, p.o.) and morphine (3 mg/kg, i.p.) on the rat body weight is shown in Fig. 2. Kratom extract at the dose of 200 and 400 mg/kg and morphine significantly inhibited an increment in body weight when compared to the control ($P < 0.05$).

3.6. *Effect of kratom extract on plasma cholecystokinin*

Plasma cholecystokinin in rats that received kratom extract (50–400 mg/kg, p.o.) or morphine (3 mg/kg, i.p.) for periods of 1, 15 and 30 days was measured. Kratom extract and morphine did not affect the level of plasma cholecystokinin in any group when compared to the control (Fig. 3).

4. Discussion

Kratom is an indigenous tree of Thailand. It has been used in traditional medicine to treat diarrhea. Kratom users have complained that they experience anorexia, and constipation coupled with small blackish stools (Suwanlert, 1975). The aim of this study was to assess the effect of the methanolic extract of kratom leaves against diarrhea using a rat model with diarrhea induced by castor oil. The result of this study clearly showed that kratom extract reduced the severity of diarrhea and also the fecal weight induced by castor oil. The effect of kratom extract on the defecation frequency when the severity of the diarrhea was scored as '+' and '0' was not significantly different from the control. However when the severity of the diarrhea was scored as '++' (copious feces) kratom extract significantly reduced the total score and fecal weight in a dose dependent manner. The intestinal transit was also decreased significantly by the kratom extract in a dose dependent manner. However, the intestinal fluid in the treated groups was not affected. Loperamide, a standard drug, used to treat diarrhea significantly decreased the intestinal fluid compared to the control. The antidiarrheal effect of the kratom extract administered at between 100 and 400 mg/kg was same as that of loperamide (6 mg/kg). Loperamide is an opioid receptor agonist which can act on the μ-opioid receptors in the myenteric plexus of the large intestines. The binding of loperamide to this receptor can cause a decrease in the activity of the myenteric plexus which decreases the motility of the circular and longitudinal smooth muscles of the intestinal wall. This increases the amount of time substances remain in the intestine and allowing for more water to be absorbed out of the fecal matter. The diarrhea inducing property of castor oil is known to be due to ricinoleic acid that causes local irritation and stimulates intestinal motility (McQuaid, 2004). Its mechanism was to decrease Na^+ and K^+ absorption across the intestinal mucosa. Thus, the activity of kratom extract may be attributed to an anti-permeability action and decreased gastrointestinal motility. However the mechanism of this action has yet to be determined.

Kratom extract contains over 25 alkaloids. Mitragynine, an indole alkaloid, is known to be the most abundant active alkaloid in this plant, *Mitragyna speciosa*. Mitragynine has been reported to inhibit the electrically stimulated guinea-pig ileum through the opioid receptor since naloxone was able to reverse this inhibitory effect. However, mitragynine was 10-fold less potent than morphine (Watanabe et al., 1997). In this study, the effect of kratom extract (50–400 mg/kg) as an antidiarrheal agent *in vivo* was not antagonized by naloxone. Naloxone is known to be a competitive opioid antagonist. This compound at the dose 1 mg/kg administered subcutaneously can antagonize the effect of morphine (0.1–2.5 mg/kg) on the gastrointestinal transit *in vivo* in rats (Pourgholami and Goshadrou, 1995). In the present study, naloxone (5 mg/kg, i.p.) did not inhibit the effects of kratom extract on defecation frequency, total score, fecal weight and change in body weight. Motility in the small intestine, as in all parts of the digestive tube, is controlled predominantly by excitatory and inhibitory signals from the enteric nervous system. These local nervous signals are however modulated by inputs from the central nervous system, and a number of gastrointestinal hormones appear to affect intestinal motility to some degree. These links are from parasympathetic and sympathetic fibers that either connect the central and enteric nervous systems or connect the central nervous system directly with the digestive tract. Thus, components of kratom extract may exert their effect on other pathways in addition to the effect of mitragynine on the opioid receptors. The effects of these components have yet to be determined.

The intestinal transit was compared when kratom extract was given for periods of 1, 15 and 30 days. A single oral dose of kratom extract decreased intestinal transit in a dose dependent manner. A dose of 400 mg/kg kratom extract for 15 days was the only concentration that significantly decreased intestinal transit. Long-term treatment (30 days) of kratom extract did not decrease the intestinal transit. Seventeen percent of all kratom users experienced constipation but the problem had resolved after chewing a leaf without swallowing its fiber (Assanangkornchai et al., 2007). It may be there is some adaptation of intestinal motility to long-term treatment of kratom extract in the absence of fiber. Treatment with morphine (3 mg/kg, i.p.) did not decrease intestinal transit. The kratom extract may exert its effect on the gastrointestinal tract in the same way as loperamide or by acting on the opioid receptors.

Repeated doses of kratom extract (50 and 100 mg/kg) for 30 days did not change the increment of body weight significantly compared with the control. However kratom extract at the doses of 200 and 400 mg/kg significantly decreased the increment of body weight. The effect of kratom extract (200 and 400 mg/kg) on the body weight was the same as the effect of morphine. Morphine produces anorexia so it will affect the body weight. Mitragynine exerted its inhibitory effect on gastric acid secretion through opioid receptors. It is speculated that the mechanism of side effects such as anorexia and weight loss induced by mitragynine is related to that of its inhibitory effect on gastric acid secretion (Tsuchiya et al., 2002). High doses of kratom extract may reduce appetite in the treated groups. The regulation of appetite is an immensely complex process involving the gastrointestinal tract, many hormones, aging, and both the central and autonomic nervous systems. Cholecystokinin (CCK) acts as a physiological satiety pathway. One of the physiological actions of CCK in the gastrointestinal tract is to regulate intestinal motility. Moreover, CCK suppresses food intake by inhibiting gastric emptying (Moran and McHugh, 1982). Amphetamine is an effective anoretic agent and has been used in the clinical treatment of obesity with an emphasis on appetite control. Amphetamine inhibition of gastric emptying and intestinal transit was due in part to a mechanism associated with the hypersecretion of endogenous CCK (Doong et al., 1998). The plasma CCK in the groups treated with kratom extract (50–400 mg/kg) was not different from the control. Thus, the anoretic effect of kratom extract may be due to other factors.

5. Conclusion

Kratom extract had an antidiarrheal effect by inhibiting diarrheal frequency, total diarrheal score and fecal weight. It decreased intestinal transit. A longer-term treatment with kratom extract for 15 and 30 days did not alter the intestinal transit time. High doses of kratom extract (200–400 mg/kg) did not increase body weight beyond that of the control. They also did not affect the level of plasma CCK.

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